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Matrix Metalloproteinases, Tissue Inhibitors of Metalloproteinases and Bone Resorbing Cytokines in Synovial Fluid of Loose Artificial Hip Joints

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ABSTRACT

Purpose

To clarify the contribution of locally produced matrix metalloproteinases (MMPs), tissue inhibitors of metalloproteinases (TIMPs) and bone resorbing cytokines to aseptic loosening of artificial hip joints through the synovial fluid.

Materials and methods

Joint fluids were collected from nine cases of loose artificial hip joint at revision surgery performed due to aseptic loosening. Enzyme-linked immunosorbent assay (ELISA) was applied for quantification of MMP-1, MMP-2, MMP-3, MMP-9, TIMP-1, TIMP-2, macrophage-colony stimulating factor (M-CSF), tumor necrosis factor (TNF)-α and interleukin (IL)-6 protein levels. Enzyme amplified sensitivity immunoassay (EASIA) was applied for IL-1 β protein level quantification. To examine the presence of membrane type (MT) 1-MMP and MMP-13 semi-quantitatively, immunoblot analysis was used. To analyze proteolytic activity of MMP-2 and MMP-9, gelatin zymographic analysis was performed. For a comparative assessment of the MMP-TIMP and cytokine profile in aseptic loose artificial hip joint fluid, synovial fluids of active rheumatoid arthritis (RA) and mild osteoarthritis (OA) were similarly analyzed.

Results

In the quantitative protein level analysis of the fluid samples, MMP-1, MMP-3 and IL-6 levels of loose artificial hip joint were as low as mild OA and lower than active RA. MMP-2 and TNF-α levels were similar to mild OA and active RA. MMP-9 level was intermediate between high active RA and very low mild OA. TIMP-1, TIMP-2, M-CSF and IL-1β levels of loose artificial hip joint were the highest among the groups. Immunoblot analysis revealed the immunoreactivity of MT1-MMP and MMP-13 of loose artificial hip joint as similar to mild OA and weaker than active RA. Zymographically, MMP-2 and MMP-9 were present in each proenzyme form, with full activity retained in all the groups.

Conclusion

Aseptic loose artificial hip joint fluid was characterized by the presence of MMPs combined with more abundant TIMPs compared to active RA and mild OA fluid, which might favor MMP stabilization in an MMP-TIMP complex and thus retain their proteolytic potential. It was also characterized by high levels of M-CSF and IL-1β. This specific characteristics may represent the result of foreign body-associated biological response typical for artificial hip joins. Due to secretion of these products to the synovial fluid, they can get access to the unloose interface between bone and prosthesis, which would cause an unfavorable biological response leading to periprosthetic weakening and osteolysis. Thus, periprostheic tissue-derived, fluid-phase MMPs, TIMPs and cytokines possibly contribute to aseptic loosening of artificial hip joints through the synovial fluid.